REMARKS

Claims 1-104 are pending. Claims 105-130 are cancelled pursuant to the restriction requirement, and without prejudice to the prosecution of their subject matter in other patent applications.

Claims 3-98 are withdrawn from consideration by the Examiner in view of species election requirements. The species election requirements were timely traversed, and a Petition for Reconsideration Of Species Election Requirements is submitted herewith. Pending the decision of the Patent Office on Applicant's Petition, certain withdrawn claims are amended, as set forth in 37 C.F.R. §1.121(c)(2).

The amendments to the claims are supported by the specification and original claims, and do not constitute new matter.

Claims 1, 2 and 99-104 are rejected as indefinite and as obvious. For reasons set forth below, Applicant requests that the rejection be removed and that the claims be allowed to issue.

1. The Invention

The present invention, in the broadest sense, is captured by claim 1:

> 1. A topical medicament intended for stopping bleeding, closing a wound, or promoting wound healing in a subject in need of such treatment, comprising the following active agents in therapeutic amounts:
> (i) an agent selected from the group consisting of fibrinogen and fibrin;
> (ii) thrombin;
> (iii) a transglutaminase; and
> (iv) a serpin protease inhibitor which does not inhibit collagenase and elastase;
> wherein the active agents may be obtained from a source selected from the group of allogenic plasma, allogenic tissue, and recombinant production; and

> wherein an active substance of allogenic origin is subjected to a process selected from the group consisting of virus depletion, virus inactivation and a combination thereof; provided that where such a process is applied to the serpin protease inhibitor, it is not applied in the presence of one or more of the other active agents.

Thus, the present invention relates to compositions comprising active agents (i)-(iv), and in addition has four further aspects. First, the source of the four listed active agents may be allogenic plasma or tissue or may be recombinantly produced. Second, an active agent is subjected to one or more process that depletes and/or inactivates virus. Third, the serpin is a member of this (**ser**ine **p**rotease **in**hibitor) superfamily that does not inhibit collagenase and elastase (so that "the inhibition of proteases released by the granulocytes immigrated into the wound area is largely avoided such that the setting in of wound healing will not be impeded" (in the specification at page 3 line 22 through page 4 line 2)). Fourth, as regards the serpin component, viral depletion/activation is carried out in the absence the other active agents. As to this last feature, the specification states (at page 4 lines 3-10):

> The present invention is further based on the finding that the inhibitory activity of allogenic protease inhibitors will be preserved to a substantially better degree if the latter are subjected to virus inactivation not within a preparation containing one or several of the other active substances of the medicament, but are virus-inactivated separately from the other active substances. In this manner, it is feasible to prepare medicaments according to the invention which contain virus-inactivated allogenic protease inhibitors having sufficient activity so as to inhibit fibrinolytic enzymes in the wound bed after application of the medicament and preventing the detachment of the fibrin wound closure from the wound bed.

Claim 1 is amended to more particularly state the present invention.

2. The Claims Are Not Indefinite

Claims 1-2 and 99-104 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for reciting that the active agents "may be obtained." Claim 1, which contains the objected to phrase, has been amended to delete "may be," thereby obviating the basis for the rejection.

Accordingly, it is requested that the rejection be withdrawn.

3. The Claims Are Not Obvious

Claims 1-2 and 99-104 are rejected under 35 U.S.C. §103(a) as being unpatentable over Wadström et al, United States Patent No. 5,631,011 ("Wadström"), Redl et al. , Canadian Patent No. 2302224 ("Redl"), and Edwardson et al., United States Patent No. 5,739,288 ("Edwardson").

According to the Examiner, Wadström discloses:

> fibrin or fibrinogen in a sealant comprising thrombin, transglutaminase, and fibrinolysis inhibitors such as alpha-1 anti-trypsin, PAI-1 or PAI-2, instantly preferred serpins lacking elastase or collagenase activity . . . in combination with additional biofibers such as collagen.

The Examiner acknowledges that Wadström does not teach the use of autologous sources.

According to the Examiner, Redl discloses "a fibrinogen-based adhesive/sealant comprising fibrinogen, thrombin . . . , serum transglutaminase (Factor XIII and a fibrinolysis inhibitor) where the latter preferably is an elastase inhibitor. The Examiner acknowledges that Redl "lacks serpins lacking elastase or collagenase activity as the fibrinolytic inhibitor, autologous sources for the active ingredients or collagen, or fibrin as the other sealant agent."

Finally, Edwardson is said to "disclose the use of non-crosslinked fibrin in a fibrin-based adhesive/sealant" where the blood used to produce the sealant may be autologous, and where "[i]t is also reported that it is known in the art to add fibrinolytic inhibitors such as PAI-1 or PAI-2 (the instantly most preferred serpins) to the fibrin sealant.

The Examiner concludes:

> A person of ordinary skill in the art at the time the invention was made would have been motivated to substitute autologous sources for the active components of the fibrin adhesive/sealant of [Wadström] and [Redl] because [Edwardson discloses] them to be functionally equivalent in a fibrin adhesive or sealant save the well-known advantage of eliminating an immunological reaction. [Wadström] and [Edwardson] both disclose that the fibrinolytic inhibitors are readily selected from a small group that highlights the most preferred serpins of the instant application. Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to use autologous active ingredients, fibrin or fibrinogen, or serpins lacking collagenase or elastase activity in a fibrin-based adhesive/sealant.

Applicant respectfully disagrees, and asserts that the claims are not obvious over any of the cited references, taken singly or in combination. As explained in Section 1 of this paper, the claimed invention has a number of requirements, including the presence of active agents (i)-(iv), and four additional aspects, namely the *source* of the active agents (allogenic or recombinant), the step of *viral depletion and/or inactivation*, the *serpin's lack of collagenase and/or elastase activity* and the *separate antiviral treatment of the serpin*.

Neither the cited references nor any combination thereof disclose *or suggest* topical medicaments having the recited four components (fibrinogen or fibrin, thrombin, a transglutaminase, and a serpin) and the four characteristics set forth above.

For example, Wadström has as its primary goal the provision of fibrin-based adhesives that do not suffer from low viscosity, and as such may contain biodegradable/biocompatible polymers. Wadström does not disclose or consider treatment of its

compositions to deplete and/or inactivate viruses, nor does it teach, suggest or imply the importance of separate treatment of serpins, or the use of serpins lacking collagenase and elastase activity.

Edwardson mentions the desirability of using autologous sources to reduce the risk of transmission of infection, but does not otherwise teach a virus depletion/inactivation step. Edwardson does not teach the desirability of using serpins lacking collagenase and elastase activity, nor separate viral depletion/inactivation of serpins.

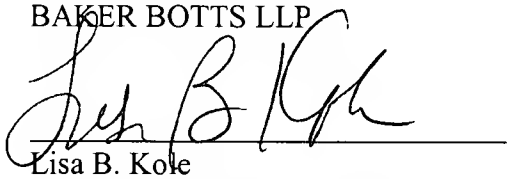
Finally, Redl focuses on the inclusion of an elastase inhibitor. Redl does teach the desirability of viral inactivation, but it does not disclose or suggest the use of serpins lacking collagenase (or arguably elastase) activities nor the separate antiviral treatment of serpin inhibitors.

Accordingly, none of the cited references, nor any combination thereof, teach or suggest all components of the claimed invention, namely a medicament comprising (i) an agent selected from the group consisting of fibrinogen and fibrin; (ii) thrombin; (iii) a transglutaminase; and (iv) a serpin protease inhibitor which does not inhibit collagenase and elastase; wherein an active substance of allogenic origin is subjected to a process selected from the group consisting of virus depletion, virus inactivation and a combination thereof; provided that where such a process is applied to the serpin protease inhibitor, it is not applied in the presence of one or more of the other active agents. Rather, each of the cited references take a different direction toward improving fibrin adhesives, with the directions being so diverse that they cannot be consider to create any motivation in the skilled artisan to produce the presently claimed invention.

3. Conclusion

For all the foregoing reasons, the pending rejections should be removed. As set forth in the accompanying Petition, and also because, for reasons set forth above, claims 1, 2 and 99-104 are patentable, claims 3-98 should be considered in this application and deemed allowable.

Respectfully submitted,
BAKER BOTTS LLP



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